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RELATIONSHIP OF THE LEUKOCYTE COUNT AND BONE MARROW CHANGES IN ACUTE LOBAR PNEUMONIA

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It is well recognized that the leukocyte count in lobar pneumonia may vary within wide limits. The majority of the cases which end fatally show either a very high or a relatively low count, while those with favorable outcome most often have counts between these extremes.[1] These points are brought out rather strikingly in the accompanying chart, showing a comparison of the leukocyte counts in 26 fatal and an equal number of recovered cases of acute lobar penumonia.

The cases with persistently low leukocyte counts may be considered first. At least two explanations for these relatively low counts have been suggested: (1) The bone marrow fails to react, either as the result of some previous injury (chronic alcoholism, for example), or on account of a paralysis of the blood-forming elements from overstimulation induced by the pneumococcus infection itself. (2) A rapid spread of the pneumococcus process results in the withdrawal of leukocytes from the blood faster than they are thrown into the circulation from the bone marrow, so that the number of circulating leukocytes may be normal or only slightly increased, in spite of the fact that the output of the bone marrow factory is far above normal. Still another possibility must be conceived, namely, that leukocytes may be formed in some other organ than the bone marrow, for example, the spleen. F. A. Evans,[2] working in this laboratory, pointed out several years ago that the gray, acute splenic tumor of lobar pneumonia contained large numbers of cells of the myeloid series, as indicated by the oxidase reaction, and suggested that the spleen might be the source of certain of the cells of the pneumonic exudate.

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[1] Osler: Principles and Practice of Medicine, Ed. 8, p. 87.

[2] Bull. Johns Hopkins Hosp., 1916, 27, p. 356.

The first explanation for the leukocyte count, namely, that the bone marrow fails to react, has been discussed by Muir, Longcope, Dickson, and others. In most of these papers the subject of acute lobar pneumonia has been considered secondarily, in connection with types of acute, nonsuppurative infections.

Muir,[3] in discussing the reaction of the bone marrow and other leukocyte-forming tissues in infection, found that the marrow pictures in his cases of acute pneumonia varied considerably. These variations he attributed to such factors as the age of the patient, the hyperplasia being less marked in late years; to the duration of the disease; to the severity of the toxemia, and to possible unknown causes such as the resisting power of the individual. He ascribed the phenomenon of depletion of adult polymorphonuclear leukocytes from the marrow to an emigration of these cells from the marrow just before death, probably in the agonal stage.

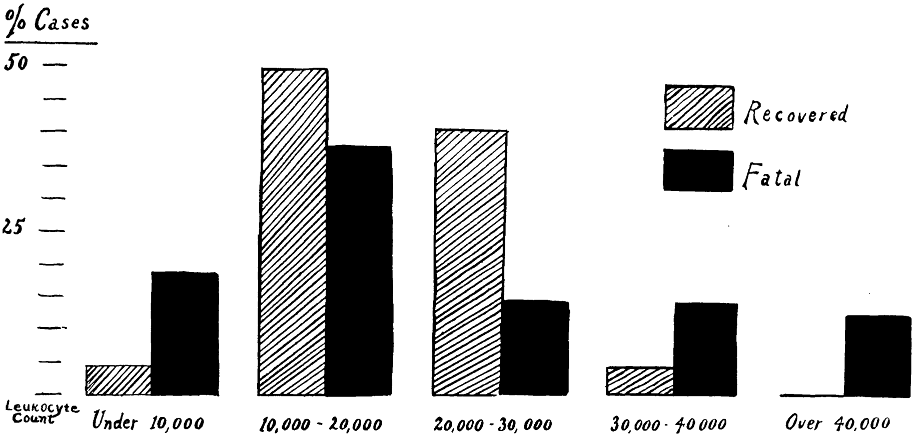

Chart 1.—Comparison of the leukocyte counts in 26 fatal and an equal number of recovered cases of acute lobar pneumonia.

The latter point was investigated experimentally by Longcope.[4] He worked with inoculated rabbits and studied their bone marrow during the course of the disease and postmortem. He explained the disappearance of the polymorphonuclear leukocytes from the marrow in any acute infection as due to a direct toxic action of the infection on the marrow, rather than to a simple emigration of the cells.

In another paper, Longcope[5] cites 2 cases of acute pneumonia in which the leukocyte count during life was below normal and the necropsies revealed an only a few cellular patches. His explanation of these observations is the possibility that the functional activity of the marrow cells in each of these patients was exhausted.

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[3] Jour. Path. and Bakteriol., 1901, 7, p. 161; Tr. Path. Soc., London, 1902, 53, p. 379.

[4] Bull. Ayer Clin. Lab. of Penn. Hosp., 1907, 4, p. 6.

[5] Bull. Ayer Clin. Lab. of Penn. Hosp., 1905, 2, p. 1.

Schurr and Löwy[6] report 2 cases of acute pneumonia that gave constant hyperleukocytic blood counts during life and yet showed aplastic, fatty marrow necropsy. These cases were used as part evidence for disproving the importance of the bone marrow as a leukocyte-former in acute infections.

Dickson,[7] in citing cases of pneumonia with leukopenic and aplastic bone marrow, ascribes the absence of leukoblastic reaction to the fact that before or during the onset of the pneumococcus infection the individual might have been weakened by alcoholic excess, syphilis, or other similar conditions. As another cause of imperfect reaction of the marrow, he describes "gelatinous degeneration" of the blood-forming tissue. This is a change in the bone marrow brought about by a progressive diminution of its blood-forming constituents along with an absorption of the fats of the marrow. This condition may be either acute or chronic.

The object of the present study was to determine, if possible, the explanation of the striking variation in the number of circulating leukocytes among cases of lobar pneumonia. We were interested particularly in finding out whether there existed a close parallelism between the leukocyte count and the degree of hyperplasia of the marrow, as has been very generally assumed. Our observations have been made on 17 cases of acute lobar pneumonia which came to necropsy. Only adults were included in the series, since in the earlier periods of life the bone marrow in the long bones is normally so active that degrees of hyperplasia cannot be easily recognized.

In every case bone marrow was obtained from the upper third of the femur. The method of procuring the specimen has been described elsewhere.[8] The tissue was fixed in Zenker's fluid, embedded in paraffin, and stained with hematoxylin and eosin. The presence or absence of hyperplasia was determined by a careful study of the microscopic sections. Aplastic marrows were classified as negative. The hyperplastic marrows were arbitrarily divided into 5 groups, designated in the table by the following signs: ±, +, + +, + + +, and + + + +. The criterion for + + + + hyperplasia was an extremely cellular marrow, replacing practically all of the adipose tissue with evidence of active cell multiplication.

A detailed study of the types of cells present in the marrow was not made, although in the routine examination of the sections it was noted, that in the majority of the cases showing hyperplasia, the predominating cell appeared to be an undifferentiated marrow cell with large round, vesicular nucleus and almost entirely fatty marrow. In 2 other similar cases there was red mottling of the marrow. In 1 case with a high leukocyte count, the marrow presented nongranular or finely granular cytoplasm. Polymorphonuclear leukocytes were present in the marrow of practically every case, and in several cases they were quite numerous. In this particular, our observations disagree with those of Muir and Longcope, to which reference was made in the previous paragraph.

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[6] Ztschr. f. Clin. Med., 1900, 40, p. 412.

[7] The Bone Marrow, 1908.

[8] Lambert, R. A.: Proc. New York Path. Soc., 1918.

The accompanying table shows the sex and age of the patients, the duration of the disease, the total and differential leukocyte count during life, and the state of the marrow at necropsy. An analysis of the data in individual cases gives varying results. In a few of the cases (Nos. 1, 4, 10 and 14) a close parallelism between the leukocyte count and the bone marrow changes is found. For example, in Case 4, in which the leukocyte count was persistently low, an aplastic marrow was found; and in Case 14, there was an association of high

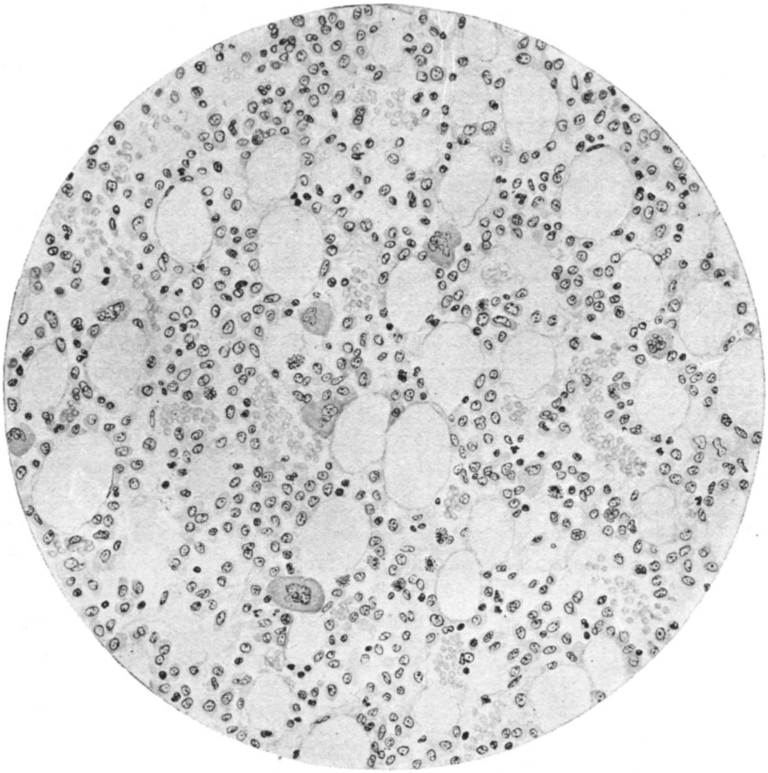

Fig. 1.—Markedly hyperplastic bone marrow from Case 17, in which the leukocyte count during life varied between 18,000 and 9,000, with a terminal count of 10,000 and 90% polymorphonuclears.

leukocyte count and a markedly hyperplastic marrow. On the other hand, in a majority of the cases, no such agreement is seen. Indeed, several cases present a striking lack of harmony between the bone marrow and blood changes. For example, Case 17 (Fig. 1), in which there was a relatively low leukocyte count, a ++++ hyperplasia of the marrow was present. This, too, in a man of 42 years, while in Case 16, showing a moderately high leukocyte count, the bone marrow was found to be aplastic.

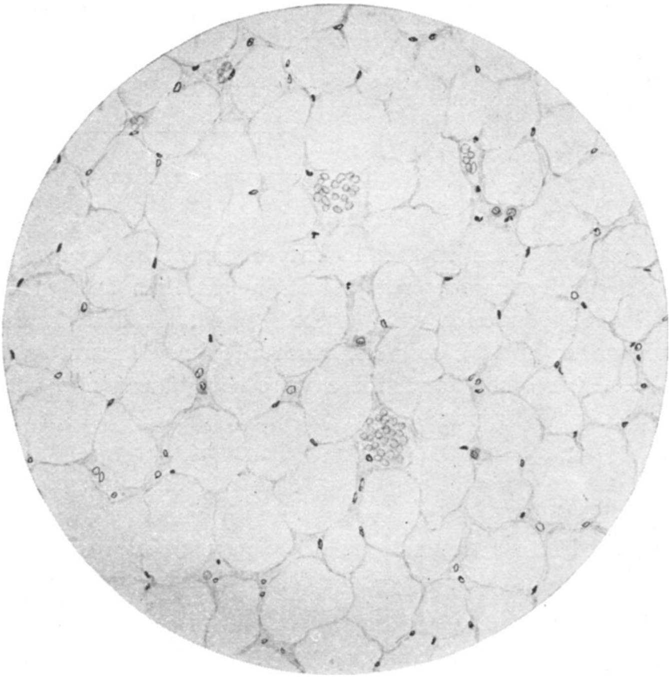

Fig. 2.—Aplastic bone marrow from Case 6, in which the leukocyte count during life varied between 17,000 and 21,000 with 90% polymorphonuclears.

An examination of the table shows that of the 17 cases, 11 exhibited varying degrees of hyperplasia of the marrow, and in 6 the marrow was aplastic. Of the aplastic cases, only one (Case 4) showed a persistently low leukocyte count. In another (Case 5), the count ranged from 28,000 to 41,000 during the earlier periods of the disease with a final count of only 4,000. In the other four cases, the counts averaged 20,000 with 90% polymorphonuclear leukocytes.

Leukocyte Count and Bone Marrow Changes in Lobar Pneumonia

Case	Sex	Age	Days Duration	Range		Final		Bone Marrow
				White Blood Cells	Polymorphonuclears	White Blood Cells	Polymorphonuclears	
1	M	39	30	17,000- 6,000	95-65	14,000	94	+
2	M	55	17	16,000-25,000	90-98	25,000	98	+++
3	M	71	16	48,000-29,000	94-92	29,000	92	+
4	M	27	5	9,000- 7,000	88-74	7,000	74	—
5	M	43	21	28,000-41,000	88-92	4,000	83	—
6	M	29	9	17,000-21,000	89-90	21,000	90	—
7	M	48	6	4,000-30,000	84-92	30,000	87	+
8	F	58	12	42,000-42,000	88-88	42.000	88	+
9	F	50	2	28,000-43,000	87-93	43,000	93	++
10	M	29	5	17,000- 4,000	92-55	4,000	55	±
11	M	48	7	12,000- 4,000	94-60	4,000	60	++
12	M	22	4	9,000-15,000	95-90	15,000	90	++
13	M	55	28	20,000-13,000	98-81	15,000	88	—
14	F	32	2	47,000-47,000	94-94	47,000	94	+++
15	M	53	1	29,000-29,000	99-99	29,000	99	+
16	M	29	4	19,000-27,000	92-93	27,000	93	—
17	M	42	9	18,000- 9,000	96-88	10,000	90	++++
Average	..	43	10	22,000-23,000	92-85	21,000	86	

SUMMARY

A close parallelism in the leukocyte count and the degree of hyperplasia of the marrow was found in less than half of 17 fatal cases of lobar pneumonia, which were studied. A few showed relatively inactive or aplastic marrows, with a leukocyte count well above normal. On the other hand, there were several cases in which the leukocyte count was persistently low during life, but in which a markedly hyperplastic marrow was found at necropsy.

To explain an aplastic femur marrow (a condition almost certainly common to all the long bones in these cases) associated with a leukocytosis during life, we may assume either a hyperplasia of the marrow of the flat bones only—a very improbable condition—or a formation of leukocytes outside the marrow, most probably in the spleen. The presence of large numbers of cells of the myeloid series in the splenic pulp would favor the latter explanation.

The cases of marked hyperplasia of the marrow with low leukocyte count are not easily interpreted. We could not find evidence in these cases of such rapid spread of the lesion as would account for a low leukocyte count through the draining of these cells out of the circulation.